Notice of Allowability	Application No.	Applicant(s)	
	09/995,791	MAERTENS ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to _____.

2. ☒ The allowed claim(s) is/are *29,31,33,35,36 and 40-51*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: The claims are seen as allowable for reasons of record, and for the reasons given below.

WO 96/04385 is cited as of interest. The patent teaches a composition containing the same components as used in the claimed method, made by the same methods. The patent discusses in very general terms immunogenic uses, partial or compete protection against HCV, an immunogenic response, prophylaxis of HCV disease. The patent does not specifically discuss the aspect of preventing a challenge infection from evolving to a chronic infection. The patent also does not provide any evidence that the disclosed compositions are effective for any aspect of protection against HCV. The state of the HCV art is highly unpredictable with regard to prophylaxis in general and specifically against chronic disease. There have been a plethora of assertions regarding prophylactic efficacy of HCV immunogens, and a dearth of evidence that the immunogens actually provide any protection in an appropriate animal model for HCV disease. Therefore, one of ordinary skill in the art would not have a reasonable expectation that the general prophylactic method suggested in the patent would have been successful. In this application, the inventors tested the composition of WO 96/04385 in a relevant animal model (see example 15). The inventors found that acute HCV disease was not prevented (ergo general prophylaxis was unsuccessful). Unexpectedly however, the acute disease failed to evolve into the chronic disease. Furthermore, the protection against chronic disease was successful in a relatively difficult real-world context, where the immunogen and the challenge came from distinct

strains of HCV. Because the inventors proved that an immunization method works for a narrower scope, which was not suggested in the prior disclosure, the instant claims are seen as novel and unobvious over the teachings of WO 96/04385.

See also the abstracts of the contemporary reviews by Alexander et al and Lechmann et al, indicating that those in the art at the time of applicant's invention viewed a successful HCV vaccine as a "remote possibility" (Alexander) and that prevention of chronic infection was highly desirable (Lechmann et al).

It is noted that claims 41 and 48 recite "wherein said E1... is produced by a recombinant host." The claims do not exclude use of E1 that was produced in a transgenic multicellular organism. However, production of proteins in transgenic plants and transgenic animals was known in the prior art. The parent claims 29, 31, and 45 all require the E1 protein to be "a single or specific oligomeric protein not disulfide linked with contaminants." The specification and the prosecution history indicate that meeting this requirement involves processing the E1 protein under particular conditions. Therefore the claims do not read upon a genetic vaccination method, or a transgenic organism per se. Considering the state of the art for recombinant production of proteins, it was concluded that there was no reasonable basis for an enablement rejection limiting the claimed method to products made in isolated recombinant cells.

Furthermore, it is noted that all of the claims refer to "E1 protein or a part thereof." The working example demonstrating prevention of chronic infection used a part of E1, the soluble portion designated E1s (amino acids 192-326). The specification teaches a number of variants of E1, including a variety of deletion variants that remove

hydrophobic segments, see Table 1. The specification discusses the importance of E1 conformational or discontinuous epitopes, teaches characterization of conformational epitopes (for a different subunit), discusses the likelihood that viral clearance from the liver (necessarily involving cellular immune response) is involved in improvements in clinical condition for chronic carriers of HCV, provides some evidence that improvement of cellular immune responses to E1 occurs during positive response to treatment in chronic carriers, further and teaches portions of the E1 protein that are involved in the cellular immune response to E1 in humans. Although the working example used only one portion of E1, it was concluded that making and using other operative portions of E1 would not require more than routine experimentation.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARY E. MOSHER, PH.D.
PRIMARY EXAMINER

12/12/05